Syllabus: Advance Diploma in Clinical Research & Pharmacovigilance

Module 1: Introduction to Clinical Research & Advancement of ICH-GCP
1.1 Clinical Research in India
• What is clinical research?
• Requirements for Global clinical research
• Clinical trial phases
• The journey towards becoming an attractive destination
• Infrastructure available
• Advantages of India
• Landmark Year 2005
• Why India is becoming a hot destination for clinical research?
• International collaboration
• Challenges ahead
1.2 Phases of Clinical Trials
• Phase-I Clinical trial & its specification
• Phase-II Clinical trial & its specification
• Phase-III Clinical trial & its specification
• Phase-IV Clinical trial & its specification
• Difference between Phase I to III & Phase IV studies
1.3 History & Background of Good Clinical Practice
• Stories behind the ethical research
• Tuskegee Syphilis Study (1932-1972)
• Outcome of Tuskegee Syphilis Study
• Belmont Report 1979
• Nazi Experiments (1940-1945)
• Outcome of Nazi Experiments
• Nuremberg Code (1947)
• Sulfanilamide Disaster (1937)
• Willowbrook study (1956)
• Thalidomide Disaster (1962)
• Outcome of Thalidomide Disaster
• Ethics
1.4 Introduction to ICH, ICH-GCP Guideline & its advancement
• ICH definition
• Why need to harmonize?
• Structure of ICH
• Different parties of ICH
• Various ICH Guidelines
• GCP definition
• ICH-GCP (E6) Guidelines
• The Principles of ICH-GCP
• Investigator
• Sponsor
• Clinical Trial Protocol & Protocol Amendment(s)

• Investigator's Brochure
• Essential Documents for Conduct of a Clinical Trial
• Integrated Addendum to ICH-GCP E6(R2)
• Indian GCP Structure & Contents
• GCP implementation
Module 2: Ethical & Regulatory Aspects of Clinical Trials
2.1 Ethics Committee
• History of unethical medical experiment
• Cleopatra's controversial experiments (69-30 BC)
• Synonyms
• EC primary purpose
• Composition of the EC
• Composition of the EC quorum
• Operational aspects of EC
• Functions of EC
• Which study needs EC permission?
• Exemption from EC
• Criteria for approval
• EC approval format
• Communication with EC during the trial
• EC Registration, re-registration & NABH accreditation
2.2 Indian Council of Medical Research
• Introduction to ICMR
• Major areas covered under guidelines
• General statements under guidelines
• Various principles under guidelines
2.3 Declaration of Helsinki
• Introduction to World Medical Association & Declaration to Helsinki (DOH)
• History of development of ethical principles for medical research involving human subjects
• General principles of DOH
• Risks, Burdens and Benefits
• Vulnerable Groups and Individuals
• Scientific Requirements and Research Protocols
• Research Ethics Committees
• Privacy and Confidentiality
• Informed Consent
• Use of Placebo
• Post-Trial Provisions
• Research Registration and Publication and Dissemination of Results
• Unproven Interventions in Clinical Practice
2.4 Drug & Cosmetic Act 1940, Schedule Y & its appendices
• Introduction to Drug & Cosmetic Act 1940 & Rules 1945
• What is Schedule Y?
• Clinical Trials & New Drug
• Investigational New Drug

• AE, ADR, SAE
• Responsibilities of Sponsor
• Responsibilities of Investigator
• Responsibilities of Ethics committee
• Regulatory structure in India
• Regulatory process
• Format of Form-44
• Human Clinical Pharmacology
• Periodic Safety Update Reports
• Bioavailability/ Bioequivalence
• Appendices of Schedule Y
• Central Drug Standard Control Organization (CDSCO)
• Clinical Trial Registry of India (CTRI)
• Online submission of clinical trial application-Sugam portal
Module 3: Operations Aspects of Clinical Trials
3.1 Clinical Trial Design
• Categories of Clinical Research
• Observational studies
• Prospective Observational studies
• Concurrent prospective studies
• Non-concurrent prospective studies
• Cross sectional prospective studies
• Retrospective Observational studies
• True Retrospective studies
• Cross sectional retrospective studies
• Experimental studies
• Community study
• Clinical Trials
• Categorization of clinical trial design
• Bias & its sources
• Control group
• Randomization
• Blinding & its type
• Sample size
• Parallel group design
• Cross over design
• Factorial design
3.2 Conduct of the study
• Moral principles
• People involved
• Sequence of activities
• Milestones in study conduct
• Essential elements of protocol
• Case record form
• Preparation of contracts
• Study start-up activities

• Study initiation
• Aspects of study conduct
• Recruitment
• Obtaining consent
• Screening
• Use of drug
• Safety Monitoring
• Withdrawal of subject
• Study site monitoring
• Study close out visit
• Quality control & quality assurance
• Audit & inspection
3.3 Data Safety Monitoring Board (DSMB)
• Introduction
• Role & Responsibilities
• Review
• Recommendations
• Membership
• Meetings
• Study Reports for DSMB Meetings
• Reports from the DSMB
• Reimbursement
3.4 Clinical Data Management (CDM)
• What is data management?
• What are data?
• Who can collect the data?
• Where is the data?
• What is a source document?
• What do you collect?
• CRF work flow
• Electronic data capture
• Manage data collection
• Data Management Plan
• Elements of data management
• Data management tool
• CRF data checks
• Data acquisitions
• Data base development & validation
• Essential characters of data base
• Coding
• Query generation
• Data base lock (soft lock, hard lock)
• Code of ethics for CDM professionals
Module 4: Pharmacovigilance at Glance
4.1 Introduction to Pharmacovigilance

• Definition of Pharmacovigilance
• Aims of pharmacovigilance
• Why pharmacovigilance is increasing?
• History of Pharmacovigilance
• Examples of product recalls due to toxicity
• Responsibilities
• Why we do need pharmacovigilance?
• Adverse Drug Reactions (ADR)
• Economic impact of ADR
• Different safety profile due to International differences
• Topics to be studied after study approval
• Changes that occur from the PV findings
• Governing bodies for Pharmacovigilance
• What should be reported?
• Who can report?
• Report to whom?
• Reporting Requirement
• International collaboration in the field of pharmacovigilance
• WHO Pharmacovigilance programme
• Pharmacovigilance programme of India (PVPI)
• Introduction
• Goals & Objectives
• Governance structure
• Steering committee
• Three layered structure
• Collaboration with WHO-UMC
• Programme communication
• Working of PvPI
• Monitoring & Evaluation
• Reporting trends
• Application/Role of Pharmacovigilance
4.2 Pharmacovigilance-Glossary and related terms
• Clinical operation-Various definitions & their brief description/concept clearance
• Pharmacovigilance- Various definitions & their brief description/concept clearance
4.3 Pharmacovigilance Methods
• Passive surveillance
• Spontaneous Reports
• Case series
• Stimulated Reporting
• Active surveillance
• Sentinel sites
• Drug event monitoring
• Registries
• Comparative Observational Studies
• Cross-Sectional Study (Survey)
• Case-Control Study

• Cohort Study
• Targeted Clinical Investigations
• Descriptive Studies
• Natural History of Disease
• Drug Utilization Study
4.4 Pharmacovigilance Data Management and Case Processing
• Importance of safety monitoring
• Sources of report
• Spontaneous report
• Literature
• Solicited sources
• Contractual agreements
• Regulatory authority sources
• Call centers
• Triage of cases
• The minimum information required for reporting purpose
• Case processing
• Data entry into safety database
• Narratives
• Medical coding
• QC review
• Medical review
• Different Pharmacovigilance Software
Module 5: Signal Management, ADR Reporting System & Dictionaries
5.1 Signal Identification, Development and Analysis
• Adverse Reaction Signal
• Factors favoring signal detection
• Speed of signal detection
• Qualitative V Quantitative signals
• Criteria for Signal Assessment
• Signal validation
• Signal strengthening
• Seriousness
• Mechanism
• Risk Groups
• Frequency determination
• Effectiveness/Risk Evaluation
• Making Decisions
• Information
• Follow-up
• Steps from Signal to Policy
5.2 Adverse Drug Reaction Reporting System
• Definition and examples of Adverse Event (AE)
• Adverse Drug Reaction (ADR)
• In the pre-approval clinical experience

• Regarding marketed medicinal products
• Unexpected Adverse Drug Reaction
• Serious Adverse Event/Reaction (SAE/R)
• Suspected Unexpected Serious Adverse Reaction (SUSAR)
• Types of ADR
• Non immunological ADR
• Immunological ADR
• Miscellaneous
• Rawlins and Thompson classification of ADRs
• Limitations of Rawlins and Thompson classification
• Wills and Brown classification of ADR
• Steps of ADR monitoring
• Assessment of ADR
• Seriousness
• Definition of Life threatening & example
• Definition of Disability & example
• Important medical events with example
• Intensity
• WHO classification
• Hartwig and Seigels scale
• Serious vs. Severe
• Relationship/Causality
• WHO Definitions
• NARANJO algorithm for assessing the causality
• Commonly used criteria for Adverse Event Relationship to Study Products
• Adverse Event Relationship to Study Products In India
• Difficulty Assessing Relationship of AEs with drug
• Expectedness/Unexpectedness
• Expected AE/R
• Unexpected AE/R
• Outcome of Adverse Events
• Reporting of ADR
• Significance of ADR reporting
• Notification of ADR
• Notification of ADR to Regulatory agency
• Types of ADR Reporting
• Standards for Expedited reporting
• Others needing expedited reporting
• Not expedited reporting
• Minimum Criteria for Reporting
• Key data elements for expedited reports
• Reporting format
• Sponsor Responsibilities
• Monitor Responsibilities
• Principal Investigator Responsibilities
• Coordinator Responsibilities
• Clinical Trial: Reporting Time Frame India
• Post Marketing Reporting Time Frame

5.3 Medical Dictionary for Regulatory Activities
• Objectives for MedDRA Development
• MedDRA and the MSSO
• MedDRA Definition
• Regulatory Status of Mandate
• MedDRA and E2B
• WHO and MedDRA
• Scope of MedDRA
• MedDRA Structure
• MSSO's MedDRA Browsers
• MedDRA Desktop Browser
• MedDRA Web-Based Browser
• MedDRA Maintenance
• Standardized MedDRA Queries (SMQs)
• SMQs in Production – Examples
• SMQ Benefits and Limitations
• SMQ Applications
• How to "Run" SMQs
• Browser Demonstration SMQ View
• MedDRA Training Resources
5.4 WHO Drug Dictionary
• General information
• Drug/Medicinal Product Classification
• The WHO Drug Dictionary (WHO-DD)
• A source of international drug names
• Medicinal product names
• Types of medicinal products in WHO-DD
• Codes and IDs
• How do we use WHO-DD
• The WHO-DD linked to ICSRs
• ATC in WHO Drug Dictionary
• ATC Classification Main Groups
• How to access the WHO-DD
• WHO Drug Dictionary – VigiSearch
• WHO Drug Dictionary – VigiFlow
• WHO Drug Dictionary- DD Browser
Module 6: Regulatory Aspects of Pharmacovigilance
6.1 Different ICH & Other requirements for Drug Safety
• E2B: Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports
• E2c: Periodic Benefit-Risk Evaluation Report (PBRER)
• E2F: Development Safety Update Report (DSUR)
• E3: Structure And Content of Clinical Study Report
• Summary of product characteristics (SmPC/SPC)
• Patient information leaflet (PIL)

• Company Core Safety Information (CCSI)
• Reference Safety Information (RSI)
• Developmental Core Safety Information (DCSI)
• The Council for International Organizations of Medical Sciences (CIOMS)
6.2 Periodic Safety Update Report (PSUR)
• Introduction
• Objectives of PSUR
• History of the PSUR
• General Principles of PSUR
• Implication of PSUR
• Sources of Information
• PSUR contents
• Quality systems for PSUR
• Training related to PSUR process
• Criteria used for defining the frequency of submission of PSURs
• Responsible parties for PSUR
• PSUR Submission Timelines
6.3 Good Pharmacovigilance Practice (GPP)
• Definition of GVP
• Guidelines on GVP
• Module III: Pharmacovigilance inspections
• Types of Pharmacovigilance inspections
• Routine pharmacovigilance inspections
• Elements to consider for Routine inspections
• For cause pharmacovigilance inspections
• Pre-authorisation inspections
• Post authorisation inspections
• Announced and unannounced inspections
• Re-inspections
• Remote inspections
• Inspection planning
• Inspection process
• Inspection follow-up
• Regulatory action
Module 7: Career orientation and Interview Preparation
7.1 Career guide
• Why we fail?
• What can make the difference?
• Why careers in clinical research can be the best choice?
• Clinical Research Domains
• Clinical Research Coordinator
• Business Development Executive
• Clinical Trial Assistant/Associate

• Statistical Analyst
• Data Coordinator
• Quality Assurance Executive
• Medical Writer
• RA-Officer
• Am I eligible to start career in Pharmacovigilance?
• How will start my career?
• How will I grow in this industry?
• Pharmacovigilance career path?
• What will be my job responsibilities?
• PV work flow
• Where I will be placed?
• When & how should I start?
7.2 Aptitude test, Group discussion & Personal Interview
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